REMARKS

Claims 11-14, 16, 20-27, 32-24, 36, 37, 44 and 50-66 are pending and under examination.

The rejection of claims 11, 13, 14, 16, 21, 22, 24-27, 32, 34, 36, 37, 44 and 50-61 under 35 U.S.C. § 102(b) as allegedly anticipated by Turner et al., Breast Cancer Res. Treatment 46:69 (1997), is respectfully traversed. Applicant respectfully maintains, for the reasons of record, that Turner et al. does not teach the claimed methods.

As discussed in the previous response, Turner et al. describes a higher percentage of overexpression of BAG-1 in cancerous invasive carcinoma (IC) (93%) and in pure ductal carcinoma *in situ* (DCIS) (80%) than in benign breast epithelium (BBE) (47%). Therefore, based on the description in Turner et al., as a tissue becomes cancerous or becomes a more aggressive form of cancer, overexpression of BAG-1 increases. As evidence that IC is a more aggressive form of cancer than DCIS, attached herewith as Exhibit 1 is a printout from the American Cancer Society's webpage providing an overview of breast cancer. As described on page 2 of Exhibit 1, DCIS is the most common type of noninvasive breast cancer. Invasive (infiltrating) ductal carcinoma is the most common form of breast cancer and, together with invasive (infiltrating) lobular carcinoma, make up about 90% of invasive breast cancers. Thus, Turner et al. describes progressively higher percentages of overexpression of BAG-1 as breast tissue goes from benign (BBE, 47%) to noninvasive breast cancer (DCIS, 80%) to invasive breast cancer (IC, 93%). In contrast, the claims recite that a high level of BAG-1 expression relative to a reference level of BAG-1 expression correlates positively with disease-free or overall survival, correlates negatively with tumor recurrence or spread, or classifies a patient as being less likely to suffer tumor metastasis or having an increased chance of survival

Furthermore, Turner et al. indicates that, in BBE, overexpression of BAG-1 was found to be in a higher proportion in the nucleus alone (30%) than in the cytoplasm and nucleus (13%) or cytoplasm alone (4%). In IC, overexpression of BAG-1 was found to be in a higher proportion in the cytoplasm alone (89%) than in the cytoplasm and nucleus (22%) or nucleus alone (4%). From their observations, Turner et al. concludes that "the subcellular location of BAG-1 overexpression may have prognostic importance with respect to survival of breast cancer patients" (emphasis added) but provides no teaching that overexpression of BAG-1 would be

prognostic for stage I or stage II breast cancer and that a high level of BAG-1 expression relative to a reference level of BAG-1 expression correlates positively with disease-free or overall survival, correlates negatively with tumor recurrence or spread, or classifies a patient as being less likely to suffer tumor metastasis or having an increased chance of survival. Thus, Turner et al. provides no teaching of methods for prognosis of breast cancer, predicting the risk of tumor recurrence or spread in an individual having a breast cancer tumor, screening a breast cancer patient to determine the risk of tumor metastasis or chance of survival, or determining the proper course of treatment for a patient suffering from breast cancer in a patient during stage I or stage II of breast cancer, as claimed.

With respect to the comments in Turner et al. on overall survival (OS) or distant disease free survival (DDFS), Turner et al. provides no indication of OS or DDFS with respect to DCIS. Regarding BBE, the description in Turner et al. relates to overexpression of BAG-1 in the nuclear component of benign tissue (BBE) and is not relevant to the claimed methods reciting stage I or stage II breast cancer. With regard to IC, Turner et al. states that the "10-year OS and DDFS for patients with overexpression of cytoplasmic BAG-1 in IC specimens was 75% and 70%, respectively, as compared with 62% and 35% for tumors with low cytoplasmic BAG-1 levels ($p=0.06$)." However, the survival difference of cytosolic staining for IC was not statistically significant at $p=0.06$. In corroboration that this was not statistically significant, attached herewith as Exhibit 2 is a Rule 132 Declaration by the inventor, Dr. John C. Reed. Dr. Reed attests that the survival difference of cytosolic staining for IC was not statistically significant and that Turner et al. failed to show a significant correlation of BAG-1 expression in breast cancer cells with patient survival. Absent such a teaching, Applicant respectfully submits that Turner et al. cannot anticipate the claimed methods.

For the reasons of record and as discussed above, and further as corroborated by the Rule 132 Declaration submitted herewith, Applicant respectfully maintains that Turner et al. does not teach the claimed methods. Absent such a teaching, Turner et al. cannot anticipate the claims. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

The rejection of claims 11-14, 16, 21, 22, 24-27, 32-34, 36, 37, 44 and 50-61 under 35 U.S.C. § 103 as allegedly obvious over Turner et al., *supra*, in view of Sano et al., U.S. Patent

No. 5,665,539, is respectfully traversed. Applicant respectfully maintains, for the reasons of record, that Turner et al., alone or in combination with Sano et al., does not teach or suggest the claimed methods.

As discussed above, Applicant respectfully maintains that Turner et al. does not teach or suggest the claimed methods. Furthermore, Applicant respectfully maintains that Sano et al. does not cure the deficiencies of Turner et al. Therefore, Applicant respectfully maintains that the claimed methods are unobvious over Turner et al., alone or in combination with Sano et al. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

The rejection of claims 11, 13, 14, 16, 20-22, 24-27, 32, 34, 36, 37, 44 and 50-66 under 35 U.S.C. § 103 as allegedly obvious over Turner et al., *supra*, in view of Sauter et al., Br. J. Cancer 76:494-501 (1997), is respectfully traversed. Applicant respectfully maintains, for the reasons of record, that Turner et al., alone or in combination with Sauter et al., does not teach or suggest the claimed methods.

As discussed above, Applicant respectfully maintains that Turner et al. does not teach or suggest the claimed methods. Furthermore, Applicant respectfully maintains that Sauter et al. does not cure the deficiencies of Turner et al. Therefore, Applicant respectfully maintains that the claimed methods are unobvious over Turner et al., alone or in combination with Sauter et al. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

The rejection of claims 11, 13, 14, 16, 21-27, 32, 34, 36, 37, 44 and 50-61 under 35 U.S.C. § 103 as allegedly obvious over Turner et al., *supra*, in view of Takayama et al., Cancer Res. 58:3116-3131 (1998), is respectfully traversed. Applicant respectfully maintains, for the reasons of record, that Turner et al., alone or in combination with Takayama et al., does not teach or suggest the claimed methods.

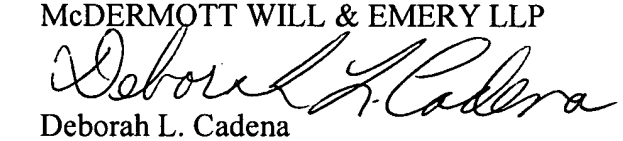
As discussed above, Applicant respectfully maintains that Turner et al. does not teach or suggest the claimed methods. Furthermore, Applicant respectfully maintains that Takayama et al. does not cure the deficiencies of Turner et al. Therefore, Applicant respectfully maintains that the claimed methods are unobvious over Turner et al., alone or in combination with Takayama et al. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

In light of the amendments and remarks herein, Applicant submits that the claims are now in condition for allowance and respectfully requests a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

McDERMOTT WILL & EMERY LLP



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Cancer Reference Information

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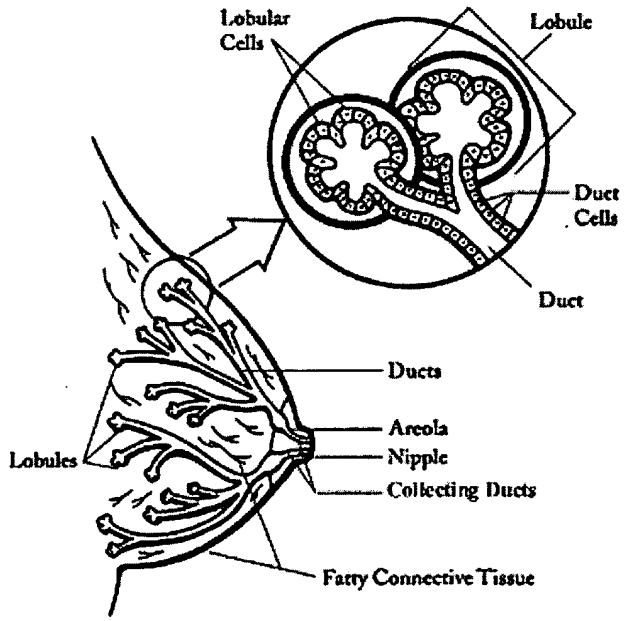
Overview: Breast Cancer

What Is Breast Cancer?

Breast cancer is a malignant (cancerous) tumor that starts from cells of the breast. The disease occurs mostly in women, but men can get breast cancer too. The information here refers only to breast cancer in women. There is separate information about breast cancer in men available in the American Cancer Society's document, "breast cancer in men."

A woman's breast is made up of glands that make breast milk (lobules), ducts (small tubes that carry milk from the lobules to the nipple), fatty and connective tissue, blood vessels, and lymph (pronounced **limf**) vessels. Most breast cancers begin in the cells that line the ducts (ductal cancer), some begin in the lobules (lobular cancer), and the rest in other tissues.



Lymph vessels are like veins, except that they carry lymph fluid instead of blood. Lymph is a clear fluid that contains immune system cells and waste products. Most lymph vessels lead to small, bean-shaped collections of tissue called lymph nodes. Most lymph vessels of the breast lead to lymph nodes under the arm. These are called axillary (**ax**-uh-lair-ee) nodes.

If breast cancer cells reach the underarm lymph nodes and continue to grow, they cause the nodes to swell. Once cancer cells have reached these nodes they are more likely to spread to other organs of the body as well.

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EXHIBIT 1

Benign Breast Lumps

Most breast lumps are benign (be-**nine**); that is, they are not cancer. Benign breast tumors are abnormal growths, but they do not spread outside of the breast and they are not life threatening. But some benign breast lumps can increase a woman's risk of getting breast cancer.

Most lumps turn out to be caused by fibrocystic (fi-bro-**sis**-tik) changes. Cysts are fluid-filled sacs. Fibrosis is the formation of scar-like tissue. Such changes can cause breast swelling and pain. The breasts may feel lumpy, and sometimes there is a clear or slightly cloudy nipple discharge. For more detail, please see the separate document, "Non-Cancerous Breast Conditions."

Main Types of Breast Cancer

Understanding key words as they relate to breast cancer can be a challenge. Here are the most common types of breast cancer:

Carcinoma in situ (in-**sigh**-to): This term is used for early stage cancer, when it is confined to the place where it started. In breast cancer, it means that the cancer is confined to the ducts or the lobules, depending on where it started. It has not gone into the tissues in the breast nor spread to other organs in the body.

Ductal carcinoma in situ (DCIS): This is the most common type of noninvasive breast cancer. DCIS means that the cancer is confined to the ducts. It has not spread through the walls of the ducts into the tissue of the breast. Nearly all women with cancer at this stage can be cured. The best way to find DCIS early is with a mammogram.

Lobular carcinoma in situ (LCIS): This condition begins in the milk-making glands but does not go through the wall of the lobules. Although not a true cancer, having LCIS increases a woman's risk of getting cancer later. For this reason, it's important that women with LCIS to follow the screening guidelines for breast cancer (see "How Is Breast Cancer Found").

Invasive (infiltrating) ductal carcinoma (IDC): This is the most common breast cancer. It starts in a milk passage or duct, breaks through the wall of the duct, and invades the tissue of the breast. From there it can spread to other parts of the body. It accounts for about 80% of invasive breast cancers.

Invasive (infiltrating) lobular carcinoma (ILC): This cancer starts in the milk glands or lobules. It can spread to other parts of the body. About 10% of invasive breast cancers are of this type.

There are also several other less common types of breast cancer. You can get information about these through our toll-free number or on our Web site (see the "How Can I Learn More" section).

Revised: 09/26/2006